## **Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application:

## **Listing of Claims:**

1. (Currently amended) An PET or SPECT in vivo imaging agent suitable for diagnostic imaging in vivo which comprises a metalloproteinase inhibitor of Formula (I) labelled with an imaging moiety attached at the Y<sup>1</sup> or Y<sup>2</sup> positions, wherein the imaging moiety can be detected following administration of said labelled matrix metalloproteinase inhibitor to the mammalian body in vivo:

$$X^3O$$
 $N$ 
 $N$ 
 $S$ 
 $Y^1$ 
 $S$ 
 $Y^2$ 
 $(I)$ 

where:

 $Y^1$  is H or -(CH<sub>2</sub>)<sub>w</sub>-(C=O)-Z; where w is an integer of value 1 to 6; and Z is OH,  $C_{1-6}$  alkoxy,  $C_{4-10}$  aryloxy or  $NR^1R^2$  wherein  $R^1$  and  $R^2$  are each independently selected from the group consisting of H,  $C_{1-6}$  alkyl,  $C_{3-6}$  cycloalkyl,  $C_{1-6}$  fluoroalkyl or  $C_{4-10}$  aryl.

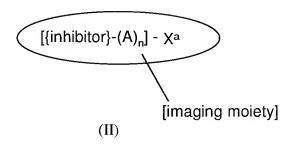
 $X^1$  and  $X^2$  together with the carbon atom to which they are attached, form a  $C_{3-10}$  saturated ring which may be alicyclic or bicyclic, and may optionally incorporate 1 or 2 heteroatoms chosen from O, N and S;

 $X^3$  is H,  $C_{1-3}$  alkyl or  $C_{1-3}$  fluoroalkyl;

 $Y^2$  is a group of formula  $-[A^1]_p[O]_qA^2$  where p and q are 0 or 1, and  $A^1$  is  $C_{1-10}$  alkylene,  $C_{3-8}$  cycloalkylene,  $C_{1-10}$  perfluoroalkylene,  $C_{6-10}$  arylene or  $C_{2-10}$ 

heteroarylene, and  $A^2$  is H,  $C_{1-10}$  alkyl,  $C_{3-8}$  cycloalkyl,  $C_{1-10}$  perfluoroalkyl,  $C_{6-10}$  aryl or  $C_{2-10}$  heteroaryl, with the proviso that when p=0, q is also 0 and  $A^2$  is not H; wherein the imaging moiety can be detected following administration of said labelled matrix metalloproteinase inhibitor to the mammalian body *in vivo*: and is chosen from:

- (i) <u>a radioactive metal ion, which is a gamma emitter or a positron emitter</u> chosen from <sup>99m</sup>Tc, <sup>111</sup>In, <sup>64</sup>Cu, <sup>67</sup>Cu, <sup>67</sup>Ga or <sup>68</sup>Ga;
- (ii) the gamma-emitting radioactive halogen <sup>123</sup>I;
- (iii) <u>a positron-emitting radioactive non-metal chosen from <sup>18</sup>F, <sup>11</sup>C or <sup>13</sup>N.</u>
- 2. (Original) The imaging agent of Claim 1, where  $Y^1$  is  $-(CH_2)_w$ -(C=O)-Z and w is 1, 2 or 3.
- 3. (Withdrawn) The imaging agent of Claim 1, where X<sup>3</sup> is H, CH<sub>3</sub> or CH<sub>2</sub>F.
- 4. (Previously presented) The imaging agent of Claim 1 where  $Y^2$  is  $-C_6H_4$ -O-A<sup>2</sup>, and A<sup>2</sup> is  $C_{6-10}$  aryl.
- 5. (Withdrawn) The imaging agent of Claim 1, where the imaging moiety is chosen from:
  - (i) a radioactive metal ion;
  - (ii) a paramagnetic metal ion;
  - (iii) a gamma-emitting radioactive halogen;
  - (iv) a positron-emitting radioactive non-metal;
  - (v) a hyperpolarised NMR-active nucleus;
  - (vi) a reporter suitable for *in vivo* optical imaging;
  - (vii) a β-emitter suitable for intravascular detection.
- 6. (Previously presented) The imaging agent of Claim 1, where the imaging agent is of Formula II:



where:

{inhibitor} is the metalloproteinase inhibitor of Formula (I);

-(A)<sub>n</sub>- is a linker group wherein each A is independently -CR<sub>2</sub>-, -CR=CR-, -

 $C \equiv C^-$ ,  $-CR_2CO_{2^-}$ ,  $-CO_2CR_{2^-}$ ,  $-NRCO_{-}$ ,  $-CONR_{-}$ ,  $-NR(C \equiv O)NR_{-}$ , -

NR(C=S)NR-,  $-SO_2NR$ -,  $-NRSO_2$ -,  $-CR_2OCR_2$ -,

-CR<sub>2</sub>SCR<sub>2</sub>- , -CR<sub>2</sub>NRCR<sub>2</sub>- , a C<sub>4-8</sub> cycloheteroalkylene group, a C<sub>4-8</sub> cycloalkylene group, a C<sub>5-12</sub> arylene group, or a C<sub>3-12</sub> heteroarylene group, an amino acid, a sugar or a monodisperse polyethyleneglycol (PEG) building block;

R is independently chosen from H,  $C_{1-4}$  alkyl,  $C_{2-4}$  alkenyl,  $C_{2-4}$  alkynyl,  $C_{1-4}$  alkoxyalkyl or  $C_{1-4}$  hydroxyalkyl;

n is an integer of value 0 to 10; and

and  $X^a$  is H, OH, Hal, NH<sub>2</sub>,  $C_{1-4}$  alkyl,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkoxyalkyl,  $C_{1-4}$  hydroxyalkyl or  $X^a$  is the imaging moiety.

- 7. (Withdrawn) The imaging agent of Claim 6, where the imaging moiety is attached at the  $Y^1$  or  $Y^2$  positions of the metalloproteinase inhibitor.
- 8. (Currently amended) The imaging agent of Claim 1, where the matrix metalloproteinase inhibitor is conjugated to a ligand, and said ligand forms a metal complex with an imaging moiety which is a radioactive metal ion or paramagnetic metal ion as defined in options (i) and (ii) of claim 5.
- 9. (Original) The imaging agent of Claim 8, where the ligand is a chelating agent.

- 10. (Withdrawn) The imaging agent of Claim 8, where the radioactive metal ion is a gamma emitter or a positron emitter.
- 11. (Withdrawn) The imaging agent of Claim 10, where the radioactive metal ion is <sup>99m</sup>Tc, <sup>111</sup>In, <sup>64</sup>Cu, <sup>67</sup>Cu, <sup>67</sup>Ga or <sup>68</sup>Ga.
- 12. (Withdrawn) The imaging agent of Claim 5, where the gamma-emitting radioactive halogen imaging moiety is <sup>123</sup>I.
- 13. (Withdrawn) The imaging agent of Claim 10, where the positron-emitting radioactive non-metal is chosen from <sup>18</sup>F, <sup>11</sup>C or <sup>13</sup>N.
- 14. (Withdrawn) The imaging agent of Claim 1, where the matrix metalloproteinase inhibitor is of Formula IV:

$$(CH_2)_w(CO)Z$$
 $X^3O$ 
 $N$ 
 $CH_2$ 
 $CH_2$ 
 $CH_2$ 
 $O$ 
 $Y^2$ 
 $(IV)$ 

where: Y<sup>2</sup>, w and Z are as defined in Claim 1;

X<sup>3</sup> is H, CH<sub>3</sub> or CH<sub>2</sub>F;

 $X^4$  is  $-(CH_2)_{m}$ - where m is 1, 2 or 3,  $-CH_2OCH_2$ - or  $X^5$  where  $X^5$  is

where t is 2 or 3.

- 15. (Withdrawn) The imaging agent of Claim 14, where Z is NR<sup>1</sup>R<sup>2</sup>.
- 16. (Previously presented) The imaging agent of Claim 1, where the matrix metalloproteinase inhibitor is of Formula V:

$$(CH_2)_w(CO)Z$$

$$HO \bigvee_{CH_2 \quad CH_2 \quad O} \bigvee_{CH_2 \quad CH_2 \quad O} \bigvee_{CH_2 \quad CH_2 \quad O} \bigvee_{(V)}$$

where:

 $X^6$  is Hal,  $R^1$  or  $OR^1$ , where  $R^1$  is  $C_{1-3}$  alkyl or  $C_{1-3}$  fluoroalkyl.

- 17. (Original) The imaging agent of Claim 16, where Z is  $NR^1R^2$ ,  $X^6$  is F; and  $X^4$  is  $-(CH_2)_2$ -,  $-CH_2OCH_2$  or  $X^5$  with t equal to 2.
- 18. (Withdrawn) A pharmaceutical composition which comprises the imaging agent of Claim 1 together with a biocompatible carrier, in a form suitable for mammalian administration.
- 19. (Currently amended) A radiopharmaceutical composition which comprises the imaging agent of Claim 1 where the imaging moiety is radioactive, together with a biocompatible carrier, in a form suitable for mammalian administration.
- 20. (Original) The radiopharmaceutical composition of claim 19, where the imaging moiety comprises a radioactive metal ion.

- 21. (Original) The radiopharmaceutical composition of claim 19, where the imaging moiety comprises a positron-emitting radioactive non-metal or a gamma-emitting radioactive halogen.
- 22. (Currently amended) A conjugate of a matrix metalloproteinase inhibitor of Formula (I) as defined in Claim 1 with a ligand, wherein said ligand is capable of forming a metal complex with an imaging moiety which is a radioactive or paramagnetic metal ion as defined in options (i) and (ii) of claim 5.
- 23. (Previously presented) The conjugate of Claim 22, of Formula IIb:

where {inhibitor}, A and n are as defined in Claim 6; and  $X^b$  is H, OH, Hal, NH<sub>2</sub>,  $C_{1-4}$  alkyl,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkoxyalkyl,  $C_{1-4}$  hydroxyalkyl or  $X^b$  is the ligand.

24. (Previously presented) The conjugate of Claim 22, wherein the matrix metalloproteinase inhibitor is of Formulae IV

$$(CH_2)_w(CO)Z$$
 $X^3O$ 
 $N$ 
 $S$ 
 $CH_2$ 
 $CH_2$ 
 $O$ 
 $Y^2$ 
 $(IV)$ 

where:  $Y^2$ , w and Z are as defined in Claim 1;

 $X^3$  is H, CH<sub>3</sub> or CH<sub>2</sub>F;

 $X^4$  is  $-(CH_2)_{m^-}$  where m is 1, 2 or 3,  $-CH_2OCH_2$ - or  $X^5$  where  $X^5$  is

-CH-O-CH- 
$$(CH_2)_t$$

where t is 2 or 3 or wherein the matrix metalloproteinase inhibitor is of Formulae V

$$(CH_2)_w(CO)Z$$

$$HO \bigvee_{CH_2 \ CH_2 \ O} \bigvee_{CH_2 \ CH_2 \ O} \bigvee_{(V)} \bigvee_{X_4} \bigvee_{X_6}$$

where:

 $X^6$  is Hal,  $R^1$  or  $OR^1$ , where  $R^1$  is  $C_{1\text{--}3}$  alkyl or  $C_{1\text{--}3}$  fluoroalkyl.

- 25. (Previously presented) The conjugate of Claim 22, wherein the ligand is a chelating agent.
- 26. (Original) The conjugate of Claim 25, wherein the chelating agent has a diaminedioxime,  $N_2S_2$ , or  $N_3S$  donor set.
- 27. (Previously presented) A kit for the preparation of the radiopharmaceutical composition of Claim 20.

- 28. (Previously presented) The kit of Claim 27, where the radioactive metal ion is <sup>99m</sup>Tc, and the kit further comprises a biocompatible reductant.
- 29. (Previously presented) A kit for the preparation of the radiopharmaceutical composition of Claim 21, which comprises a precursor, said precursor being a non-radioactive derivative of the matrix metalloproteinase inhibitor of wherein said non-radioactive derivative is capable of reaction with a source of the positron-emitting radioactive non-metal or gamma-emitting radioactive halogen to give the desired radiopharmaceutical.
- 30. (Original) The kit of claim 29 where the precursor is in sterile, apyrogenic form.
- 31. (Previously presented) The kit of Claim 29, where the source of the positron-emitting radioactive non-metal or gamma-emitting radioactive halogen is chosen from:
  - (i) halide ion or  $F^+$  or  $I^+$ ; or
  - (ii) an alkylating agent chosen from an alkyl or fluoroalkyl halide, tosylate, triflate or mesylate.
- 32. (Withdrawn) The kit of Claim 29, where the non-radioactive derivative is chosen from:
  - (i) an organometallic derivative such as a trialkylstannane or a trialkylsilane;
  - (ii) a derivative containing an alkyl halide, alkyl tosylate or alkyl mesylate for nucleophilic substitution;
  - (iii) a derivative containing an aromatic ring activated towards nucleophilic or electrophilic substitution;
  - (iv) a derivative containing a functional group which undergoes facile alkylation;
  - (v) a derivative which alkylates thiol-containing compounds to give a thioethercontaining product.
- 33. (Previously presented) The kit of Claim 29, where the precursor is bound to a solid phase.

- 34. (Withdrawn) A method of diagnostic imaging of atherosclerosis of a mammalian subject *in vivo*, which comprises administration of the imaging agent of Claim 1 to said subject, followed by detection of the imaging moiety of said imaging agent.
- 35. (Withdrawn) A method of diagnostic imaging of unstable plaques of a mammalian subject *in vivo*, which comprises administration of the imaging agent of Claim 1 to said subject, followed by detection of the imaging moiety of said imaging agent.
- 36. (Withdrawn) A method of intravascular detection of atherosclerosis of a mammalian subject *in vivo*, which comprises administration of the imaging agent of Claim 1 to said subject, followed by detection of the imaging moiety of said imaging agent.